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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,120	06/14/2001	David Thomas Dudley	5968-01-SMH	5646

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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,120	DUDLEY ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/16/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed March 16, 2004 have been entered. The cancellation of claims 1-5 in amendments filed March 16, 2004 is acknowledged. The addition of claims 20-21 is also acknowledged.

Claims 6-21 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the instant case, the instant specification fails to provide information to one of skilled in the art to practice the method of preventing arthritis without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

The breadth of the claim is so broad that it encompasses the method of preventing every kinds of arthritic disorder. Merck Manual (The Merck Manual of Diagnosis and Therapy, 16th. ed., 1992, pages 1293-1315, 1326-1327, 1338-1343, and 1369-1371) teaches that certain kinds of arthritis are autoimmune related. Some of the arthritis are infection related, and osteoarthritis is degenerative disorders. It is well-known in the state of the art that the term "arthritis" encompasses so many different diseases from various origins and caused by different etiologies (e.g., multifactoral involving genetic, age, sex, and environmental) (See pages 1294-1295 of Merck Manual). The current known treatments of these disorders depends on the patient populations and the severity of the disorders. Moreover, treatments are mostly symptomatic (See page 1295, Treatment Section). Thus, it is clear from the evidence of the Merck Manual that the ability to treat and or prevent arthritis is highly unpredictable and has met with very little success. Applicants have not provided any convincing evidence such as working examples that their claimed invention is indeed useful as preventive for arthritis and have not provided sufficient guidance to allow one skilled in the art to select patient, without arthritic disorders and otherwise healthy, to receive the herein claimed treatment for the prevention of arthritis. The instant specification fails to

provide information to one of skilled in the art to practice the claimed invention without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 15-16 are rejected under 35 U.S.C. 102(a) as being anticipated by Bridges et al. (WO 98/37881), reference of record.

Bridges teaches a method of administering the herein claimed compounds to treat septic shock (See claims 1 and 9).

Claims 15-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Barrett et al. (US patent 6,251,943).

Barrett et al. teaches a method of administering the herein claimed compounds to treat septic shock (See claims 1 and 9).

Applicants' attention is directed to *Ex parte Novitski*, 26 USPQ2d 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a *haec verba* recitation for such utility. In the instant application, as in *Ex parte Novitski*, supra, the claims are directed to preventing a malady or disease with old and well known compounds or compositions. It is now well settled law that administering compounds inherently possessing a protective utility anticipates claims directed to such protective use. Arguments that such protective use is not set forth *haec verba* are not probative. Prior use for the same utility clearly anticipates such utility, absent limitations distancing the proffered claims from the inherent anticipated use. Attempts to distance claims from anticipated utilities with specification limitations will not be successful. At page 1391, *Ex parte Novitski*, supra, the Board said "We are mindful that, during the patent examination, pending claims must be interpreted as broadly as their terms reasonably allow. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). As often stated by the CCPA, "we will not read into claims in pending applications limitations from the specification." *In re Winkhaus*, 52 F.2d 637, 188 USPQ 219 (CCPA 1975).". In the instant application, Applicants' failure to distance the proffered claims from the anticipated prophylactic utility, renders such claims anticipated by the prior inherent use.

The deletion of limitations directed to preventing arthritis would be favorably considered by the examiner to obviate the rejection under 35 USC 102.

The rejection set forth below is directed to the treatment of arthritis.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 6-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scherle et al. (The Journal of Immunology, 1998 Oct;161:5681-5686) and McGilvray et al. (The Journal of Biological Chemistry, 1997; 272(15): 10287-10294) in view of Bridges (WO 98/37881 from the International Search Report).

Scherle et al. teaches a MEK inhibitor, U0126, as effective in inhibiting the production of proinflammatory cytokines, such as IL-1, IL-8, TNF, and prostaglandin E2 (See the abstract and apge 5684, col. 2, first paragraph).

McGilvray et al. teaches the involvement of MAP kinase (MEK) pathway in the activation of monocytic cells during transmigration to inflammatory sites (See the abstract). McGilvray et al. teaches the selective inhibition of MAP kinase by MEK-1 inhibitor, PD98059, being useful for blocking and interrupting the adhesion and recruitments of human monocytes and thereby modulating the inflammatory response (See the abstract and page 10287, col. 2, second paragraph).

The primary references do not expressly teach the active compounds herein to be MEK inhibitors useful for the treatment of arthritis.

Bridges teaches that the active compounds herein are MEK inhibitors (See page 3, line 16 – page 22, line 29). Bridges also teaches the specific MEK inhibitor recited in claim 17 herein as a preferred MEK inhibitor (See page 22, line 24-25).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the MEK inhibitors of Bridges to treat arthritis such as osteoarthritis and rheumatoid arthritis.

One of ordinary skill in the art would have been motivated to employ the MEK inhibitors of Bridges to treat arthritis such as osteoarthritis and rheumatoid arthritis: the activation of MEK is known to be involved in reducing the inflammatory process, such as production of inflammatory cytokines and prostaglandin E2, interpretation of adhesion and recruitments of monocytes to the inflammatory sites, in the body. Furthermore, the inhibition of MEK is known to 1) suppress the production and release of pro-inflammatory cytokines such as interleukin-1β, PGE2, TNF, and interleukin-8; and 2) block and interrupt the adhesion of monocytes to the inflammatory sites. Possessing

the teachings of the prior art the skilled artisan would therefore employ any known MEK inhibitors, including those MEK inhibitors of Bridges, to treat arthritis such as rheumatoid arthritis and osteoarthritis, absent evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Patent Examiner
Art Unit 1617